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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/006,999 | 01/14/1998 | CLIVE J. SHIFF | PMS241460 | 4395 |

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| EXAMINER |
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CYGAN, MICHAEL T

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| ART UNIT | PAPER NUMBER |
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2856

DATE MAILED: 12/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/006,999

Applicant(s)

SHIFF ET AL.

Examiner

Michael Cygan

Art Unit

2856

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4,6-8 and 10-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4,6-8 and 10-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☒ Interview Summary (PTO-413) Paper No(s). 22.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. 6) ☐ Other:

DETAILED ACTION

Status of Application

1. The instant application has been remanded from the Board of Patent Appeals and Interferences (BPAI). The final rejection of paper 13 has been vacated, thus ending the appeal and returning jurisdiction over the application to the examiner. No ultimate position has been taken by the board on the correctness of the vacated rejections. See Ex parte Zambrano 58 USPQ 2d 1312, 1313. A rejection not inconsistent with the views expressed in the opinion follows.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Mudambi (Proceed. 26th Conf. Great Lakes Res., May 1983). Mudambi discloses a continuous flow apparatus comprising a continuous flow centrifuge and a XAD-8 filtration column. XAD-8 is a particulate material composed of micron-sized polyaromatic particles, disclosed here to be

packed into a column which restricts large-diameter molecules from passing through.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1, 4, 6-8, and 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitmore (Wat. Sci. Tech. 1993) in view of Olsson (US 5,019,497). Whitmore discloses the claimed invention, a continuous flow centrifuge and method for using the centrifuge to recover cryptosporidium from water (pages 69 and 72), except for the use of a particulate column in the centrifuge apparatus. Olsson teaches the use of a particulate column (Sephadex) mounted in a centrifuge tube to catch the flow through containing a desired sample material (column 7, lines 10-23). It would have been obvious to use a particulate column as taught by Olsson in the invention taught by Whitmore to filter the desired material (cryptosporidium) from water, since this would eliminate the tedious deposit transferal steps (involving scraping material from the centrifuge and rinsing with water). Further motivation is provided by Whitmore in the

abstract, which states that "continuous flow centrifuges tested were not shown to be capable of yielding satisfactory recoveries, although it is considered more refined machines currently available may warrant investigation"; thus pointing for the need for an improved centrifugation recovery apparatus.

With respect to the choice of particulate material for cryptosporidium, Whitmore teaches that sand can be used as a particulate filter which retains cryptosporidium (page 71). It would have been obvious to use sand as taught by Whitmore as the particulate filter material as taught by Whitmore in view of Olsson, since sand is shown to retain the desired material (cryptosporidium).

With respect to claims 10-11, the claimed invention is taught by Whitmore in view of Olsson as stated above, except for the size ranges stated. It would have been obvious to one having ordinary skill in the art at the time the invention was made to use sand of 200-50 micrometers or 120-50 micrometers, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum of workable ranges involves only routine skill in the art. See *In re Aller*, 105 USPQ 233. Additionally, in *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the

claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

4. Claims 1, 4, 6-8, and 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borschardt (US 5,846,439) in view of Leu (US 5,866,071). Borschardt teaches a continuous flow centrifuge (column 3, lines 64-67) used to filter *Cryptosporidium* oocysts from a solution (column 4, lines 37-55).

With respect to claim 1, Borschardt teaches the claimed invention except for the use of a particulate filtration column. Leu teaches the use of a particulate filtration column in a centrifuge (figures 4a, 4b, 4c; column 2, lines 62-65; column 3, lines 4-9 and 27-40) to enhance the separation abilities of the centrifuge (column 1, lines 13-23). In the apparatus of Leu. In the apparatus of Leu, a column is packed with finely divided dextran particles (column 4, lines 35-53). The particulate material in the column consists of several different zones (d1-d5) of dextran concentration. When sample material (P0), such as cellular solutions (column 4, lines 35-36) to be filtered is placed in the column, operation of the centrifuge forces the sample material to be forced through the dextran particulate material. The sample material (layer P0 in Figure 4a) is filtered into its constituent parts (layers P1,P2,P3 in Figure 4b) through dextran layers (d2-d4)

by the interaction of the sample with the particulate material (column 4, lines 46-50).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use the column of Leu in the continuous flow centrifuge of Borschardt since Leu states that the addition of a media column increases the separation ability of the centrifugation; during centrifugation, analytes are separated into different media according to their densities (column 3, lines 39-40). Without such a media column, centrifugation results in a pellet consisting not only of the desired cellular material, but also containing other fragmentary material which is not desired.

With respect to claims 4 and 12, Borchardt in view of Leu teaches the claimed invention as stated above except for the use of glass or sand particulate material. Borchardt discloses that it is known in the art to use sand columns to filter oocysts from water in flow systems (column 2, lines 17-31). It would be obvious to use sand columns in the centrifuge of Borschardt in replacement of the media of Leu, as sand columns are known to filter oocysts.

With respect to claims 6-8, Borschardt teaches that it is known in the art to perform microorganism, cryptosporidium in particular, concentration in a fluid stream of a continuous flow centrifuge (column 2, lines 41-42).

With respect to claims 10-11, the claimed invention is taught by Borschardt in view of Leu as stated above, except for the size ranges stated. It would have been obvious to one having ordinary skill in the art at the time the

invention was made to use sand of 200-50 micrometers or 120-50 micrometers, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum of workable ranges involves only routine skill in the art. See *In re Aller*, 105 USPQ 233. Additionally, in *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

Conclusion

5. The art made of record and not relied upon is considered pertinent to applicant's disclosure. Use of particles suspended in liquid to form a filter medium in a centrifugation tube is disclosed by Dorn (US 3,928,139 and US 4,212,948) and Contant-Pussard (US 6,020,150 and WO 96/29427). Coupling of a continuous-flow centrifuge to a filtration system is disclosed by Shafer (Ph.D. diss, May 1989).

Response to Arguments

6. In light of the comments by the members of the BPAI in paper 20 and applicant's representative in the interview of 23 October, it appears

necessary to clarify the teachings of Leu (US 5,866,071) in view of the language of the claims of the instant application; in particular, the phrase "a filtration column of particulate material".

As defined by Merriam-Webster:

Filtration: the process of *passing through* or as if through a filter.

Filter: a porous article or mass (as of paper or sand) through which a gas or liquid is passed to *separate* out matter in suspension.

Particulate: of or relating to minute separate particles.

Particle: a minute quantity or fragment; any of the basic units of matter and energy (as a *molecule*, atom, proton, electron, or photon).

In setting forth the teaching of Leu, the "filtration column of particulate material" was equated to the layers of dextran solution in the centrifuge tube. The questions, then are (1) is dextran solution a particulate material, and (2) does the dextran solution perform a filtration function.

Dextran is a particulate material. Since dextran is a minute *molecule*, it certainly qualifies as a particle. Dextran particles can be obtained (e.g., from supplier Sigma-Aldrich) at specified molecular weights for purposes such as gel permeation chromatography.

Dextran performs a filtration function. In the method of Leu at column 4, lines 35-53, a cell sample is *passed through* dextran layers such that pancreatic islets and cells

are *separated* into different dextran layers. This can be seen in Figures 4a-4b. In Figure 4a, the sample (P0) is placed between layers of dextran (d1 and d2) in a tube. After centrifugation, the sample is spread out into multiple layers (P1, P2, P3) which have passed through at least dextran layer (d2), see Figure 4b. Some components of the sample have also passed through other dextran layers (d3 and d4). If there were no dextran in the tube, the sample would not be separated into components; instead, the solids in the sample would form a hard, dense pellet in the bottom of the tube which would require further treatment to separate out desired material from undesired solid contamination. Clearly, the dextran layers filter the sample solution into a number of component layers.

For yet further proof, see U.S. 3,928,139 to Dorn, which discloses a system nearly identical to that of Leu, comprising a centrifuge tube containing a liquid sample and a dextran medium which undergoes density gradients centrifugation to separate the liquid sample into its constituent members; see column 3, lines 28-48 and column 5, lines 19-48. The dextran medium is explicitly described as a "filter medium". The centrifugation process is stated (at column 3, lines 38-41) to "force the fluid sample against the liquid filter medium and cause the microbial pathogens to selectively pass therein and thereby separate from the mass of the body fluid sample". The dextran is most certainly particulate as it is composed of particles, specifically, polymeric dextran particles "having a weight average molecular weight in the range of from about 10,000 to about 2,000,000"; see column 5, lines 39-42.

Therefore, it is indisputable that Leu teaches "a filtration column of particulate material" as applied in the rejection against the claims. While the description of dextran as being provided in units of volume at a certain percent concentration may be novel to those unfamiliar with modern analytical chemistry, the use of particles such as dextran (or Sephadex) in such a manner to separate biological macromolecules is used extensively; see page 394 of Allcock's Contemporary Polymer Chemistry.

As a further note as to the obviousness of the use of sand as a filter, the examiner notes that *even the general-audience Merriam-Webster's Collegiate Dictionary presents sand as an example of a filter.*

7. The documents requested by the BPAI have been made of record in the application, but were found to contain no relevant teachings.
8. Additional rejections are presented based upon the disclosures of Olsson (US 5,019,497) and Mudambi (Proceed. 26th Conf. Great Lakes Res., May 1983) in pursuit of thoroughness and in an effort to speed prosecution.
9. The Mudambi reference discloses the use of a particulate column composed of XAD particles (XAD-8). Information on XAD is provided from the manufacturer's website (<http://www.ionexchanger.com/Pharmaceuticals/xad.htm>).
10. The Olsson reference discloses the use of a particulate column composed of Sephadex beads (i.e., particles). Information on Sephadex is provided from the marketer's website (<http://www.sigmaaldrich.com>). Note that

Sephadex is commercially available in the 40-120 micron size range as recited in claim 11. A collegiate laboratory experiment which details the filtration process of a Sephadex column is made of record (<http://chemweb.calpoly.edu/chem/rice/csuperb/CLUES%20protocols/TWO/Lab2VerA.doc>) Note particularly pages 1 and 3 for an explanation of how Sephadex or like beads act as filtration columns.

11. As the previous rejection (paper 13) is vacated, the responses to applicant's arguments of the preceding reply (paper 12) are repeated below.
12. Applicant's arguments filed 13 June 2000 have been fully considered but they are not persuasive.
13. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., replaceable tubes and the use of 20-30 liters of water) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).
14. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion,

or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, as stated on page 3 of the previous Office Action, Leu states that the addition of a media column increases the separation ability of the centrifugation; during centrifugation, analytes are separated into different media according to their densities (column 3, lines 39-40)..

15. In response to applicant's argument that the invention of Leu cannot be bodily combined with the invention of Borchardt, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).
16. In response to applicant's argument that Borchardt teaches away from the use of sand columns, the examiner notes that sand was noted to be poor when used not in centrifugation, but rather in columns, where the flow rate posed a problem. What Borchardt teaches is that the use of sand for separating oocysts was known.

Art Unit: 2856

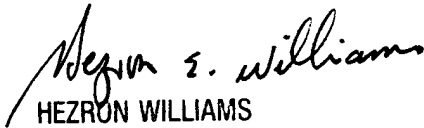
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Cygan whose telephone number is 703-305-0846. The examiner can normally be reached on 8:30-6 M-Th, alternate Fridays.

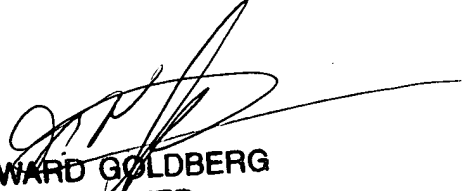
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Hezron Williams can be reached on 703-305-4705. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7722 for regular communications and 703-308-7722 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-3431.

MTC

Michael Cygan, Ph.D.
October 31, 2002


HEZRON WILLIAMS
SUPERVISORY PATENT EXAMINER
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